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DiCesare et al.

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(54) **IMPLANTABLE DRUG DELIVERY DEVICES FOR GENITOURINARY SITES**

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A61M 31/00 (2006.01)

(52) **U.S. Cl.**
CPC ***A61M 31/002*** (2013.01)

(58) **Field of Classification Search**
CPC A61M 2205/04; A61M 2210/1085; A61M 31/00; A61M 31/002; A61F 2250/0068; A61K 9/0034; A61K 9/0092
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,901,232	A	8/1975	Michaels et al.
4,016,251	A	4/1977	Higuchi et al.

(Continued)

FOREIGN PATENT DOCUMENTS

DE	3332156	A1	3/1985
EP	0572932	A2	12/1993

(Continued)

OTHER PUBLICATIONS

Giannantoni, et al., "New Frontiers in Intravesical Therapies and Drug Delivery," European Urology, vol. 50 (2006), pp. 1183-1193, Elsevier B.V.

(Continued)

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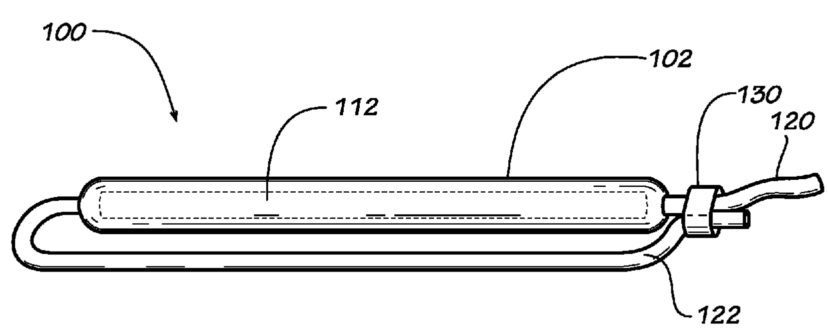
(57) **ABSTRACT**

Implantable drug delivery devices are provided lo have a deployment shape for implantation in the body and a retention shape for retention in the body. The device may have one or more elongated drug reservoirs containing a drug, mid the drug reservoir may be formed from a deformable material. In one case, a first filament is attached to the first end of the drug reservoir and second filament is attached to the second end of the drug reservoir, wherein a fastener is positioned about the first and second filaments to permit shortening and prevent lengthening of the filaments with reference to the ends of the daig reservoir, as a means for transforming the device from the implantation shape to the retention shape.

12 Claims, 15 Drawing Sheets



(56) **References Cited**

U.S. PATENT DOCUMENTS

4,475,916	A	10/1984	Himmelstein
4,871,542	A	10/1989	Vilhardt
6,039,967	A	3/2000	Ottoboni et al.
6,086,909	A	7/2000	Harrison et al.
6,171,298	B1	1/2001	Matsuura et al.
6,524,608	B2	2/2003	Ottoboni et al.
6,537,193	B1	3/2003	Lennox
7,232,421	B1	6/2007	Gambale et al.
2004/0260272	A1	12/2004	Friedman et al.
2005/0234013	A1	10/2005	Parsons
2005/0238733	A1	10/2005	Henry
2006/0105010	A1	5/2006	Rahe et al.
2006/0264912	A1	11/2006	Mcintyre et al.
2007/0172508	A1	7/2007	Zupkas et al.
2007/0202151	A1	8/2007	Lee et al.
2009/0149833	A1	6/2009	Cima et al.
2010/0003297	A1	1/2010	Tobias et al.
2010/0076261	A1	3/2010	Neeman et al.
2010/0330149	A1	12/2010	Lee et al.
2011/0060309	A1	3/2011	Lee et al.

FOREIGN PATENT DOCUMENTS

WO	98/31415	A1	2/1998
WO	99/18884	A1	4/1999
WO	00/40234	A1	7/2000
WO	01/67991	A1	9/2001
WO	02/085428	A2	10/2002
WO	03/009882	A2	2/2003
WO	2004/037318	A2	5/2004
WO	2005/072751	A1	8/2005
WO	2005/115245	A1	12/2005
WO	2006/121969	A1	11/2006
WO	2007/115259	A2	10/2007
WO	2008/038281	A2	4/2008
WO	2008/115536	A2	9/2008
WO	2009/029958	A1	3/2009

OTHER PUBLICATIONS

Henry, et al., "Topical Anesthesia of the Bladder," Abstracts, A61.

Tyagi, et al., "Local Drug Delivery to Bladder Using Technology Innovations," Urological Clinics of North America, vol. 33 (2006), pp. 519-530, Elsevier Inc.

Fraser, et al., "The Future of Bladder Control—Intravesical Drug Delivery, a Pinch of Pepper, and Gene Therapy," Reviews in Urology, vol. 4, No. 1 (2002).

Santus, et al., "Osmotic drug delivery: a review of the patent literature," Journal of Controlled Release, vol. 35 (1995), pp. 1-21.

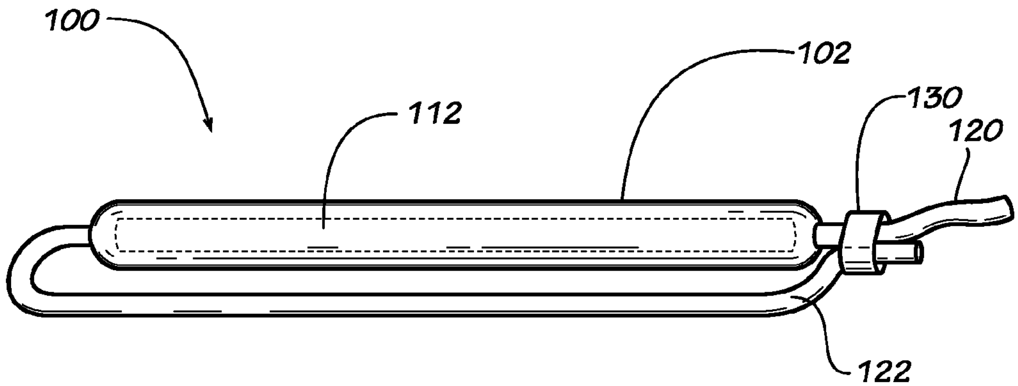


FIG. 1A

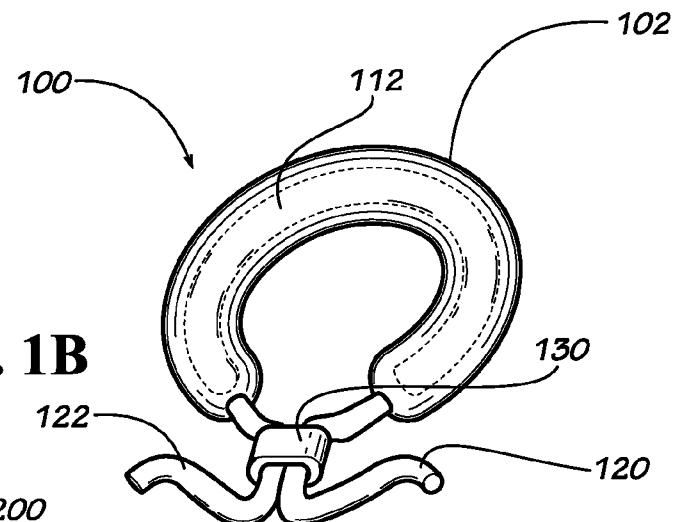


FIG. 1B

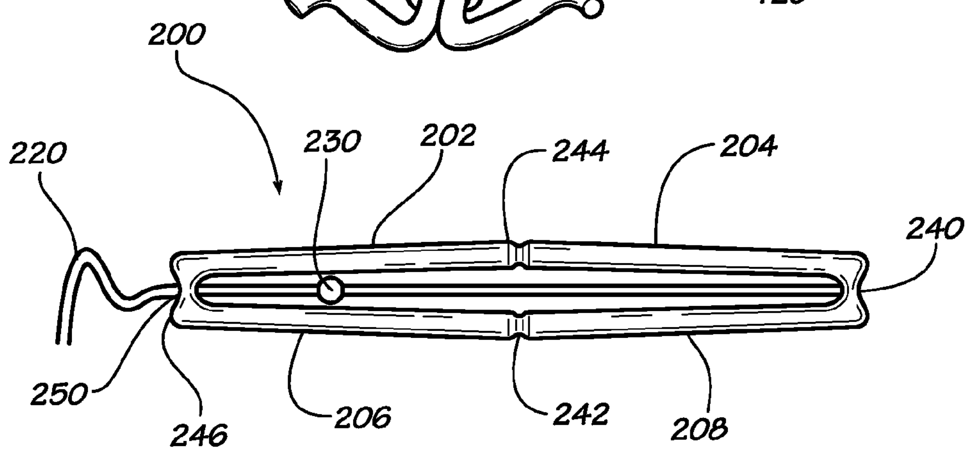


FIG. 2A

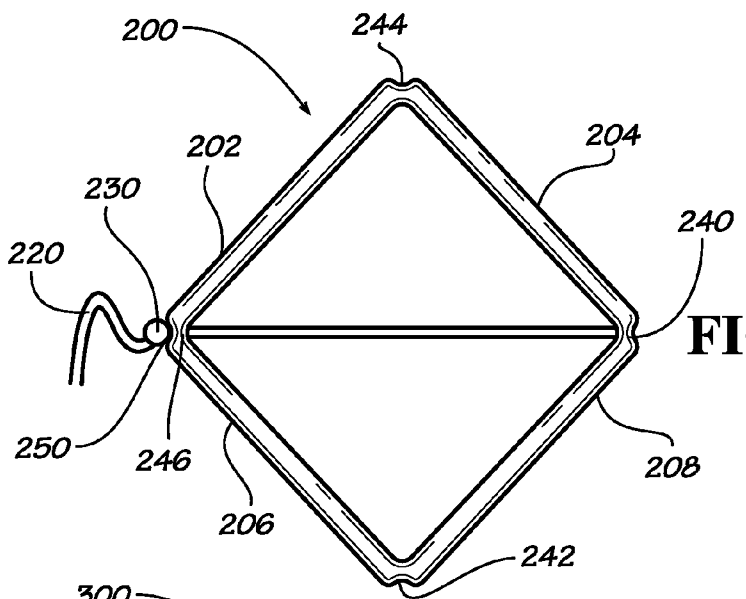


FIG. 2B

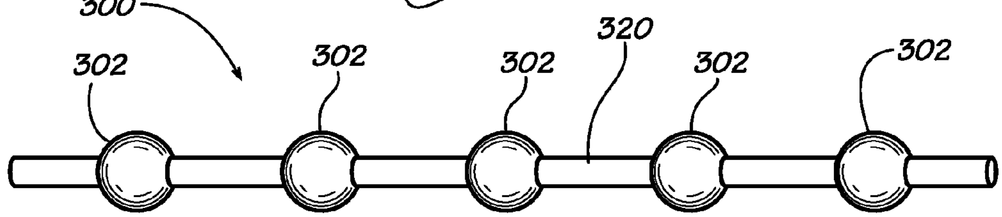


FIG. 3A

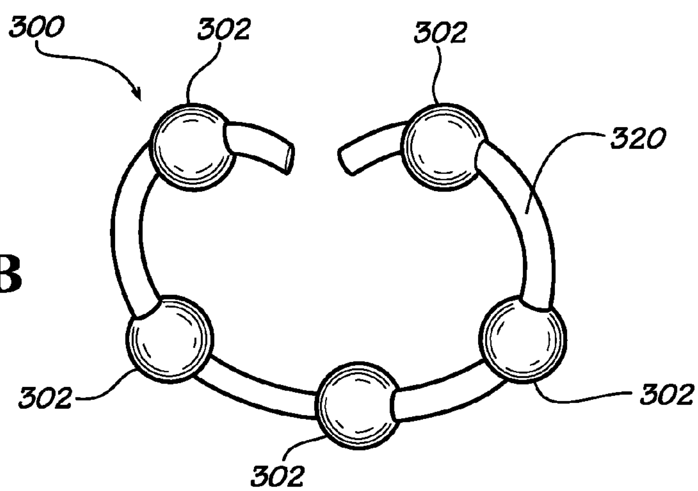


FIG. 3B

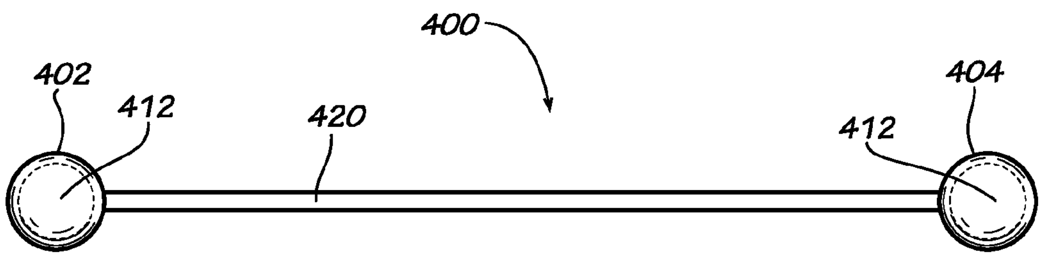
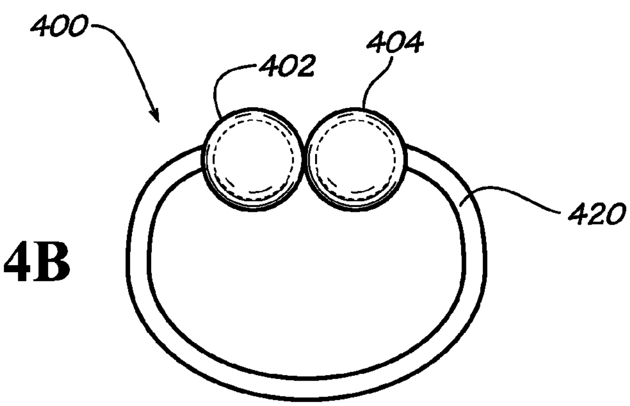


FIG. 4A

FIG. 4B



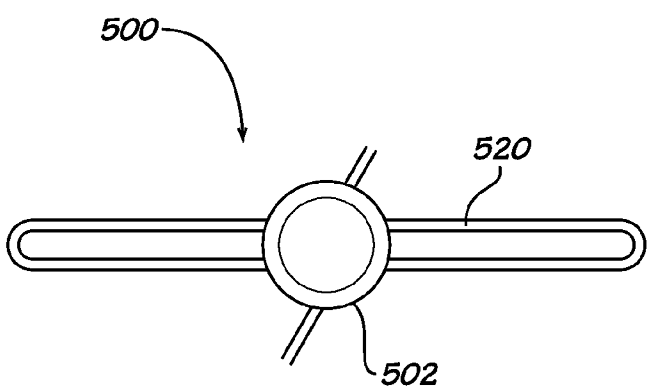


FIG. 5A

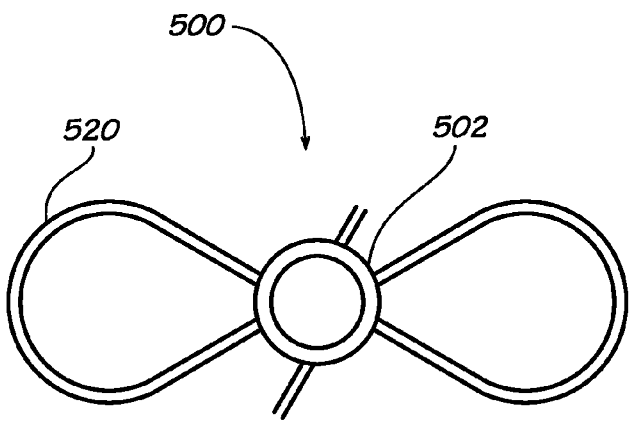


FIG. 5B

FIG. 5C

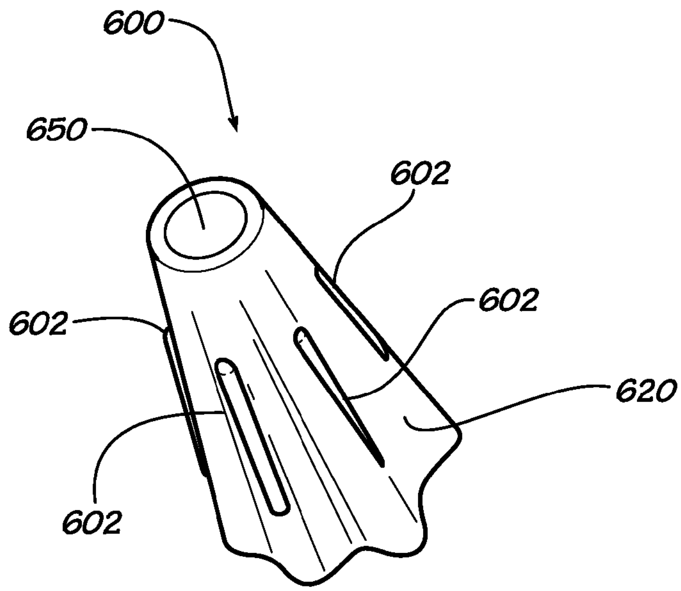


FIG. 6A

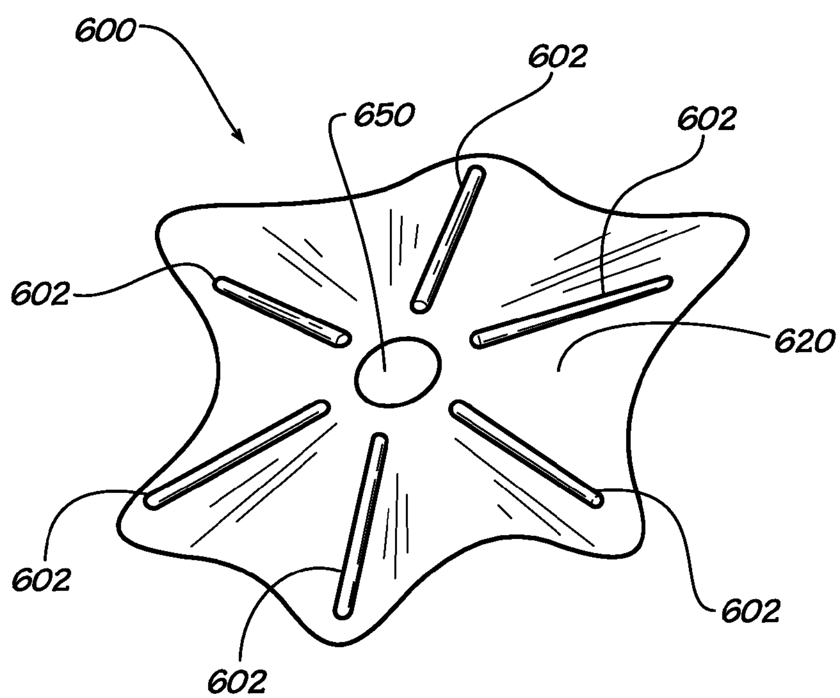
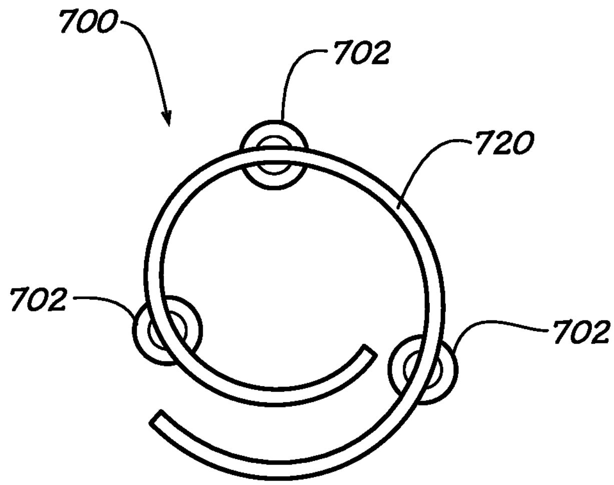


FIG. 6B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702
702

FIG. 7A

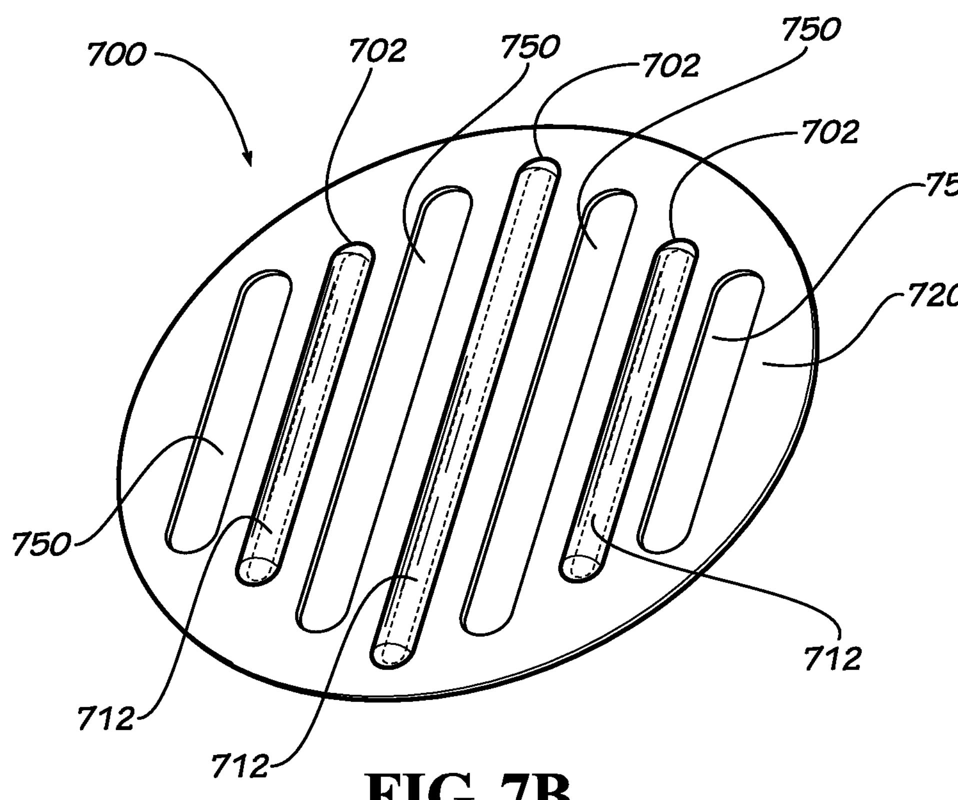
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FIG. 7B

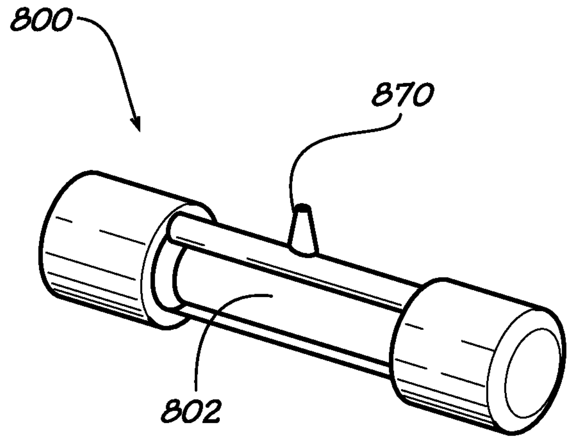


FIG. 8A

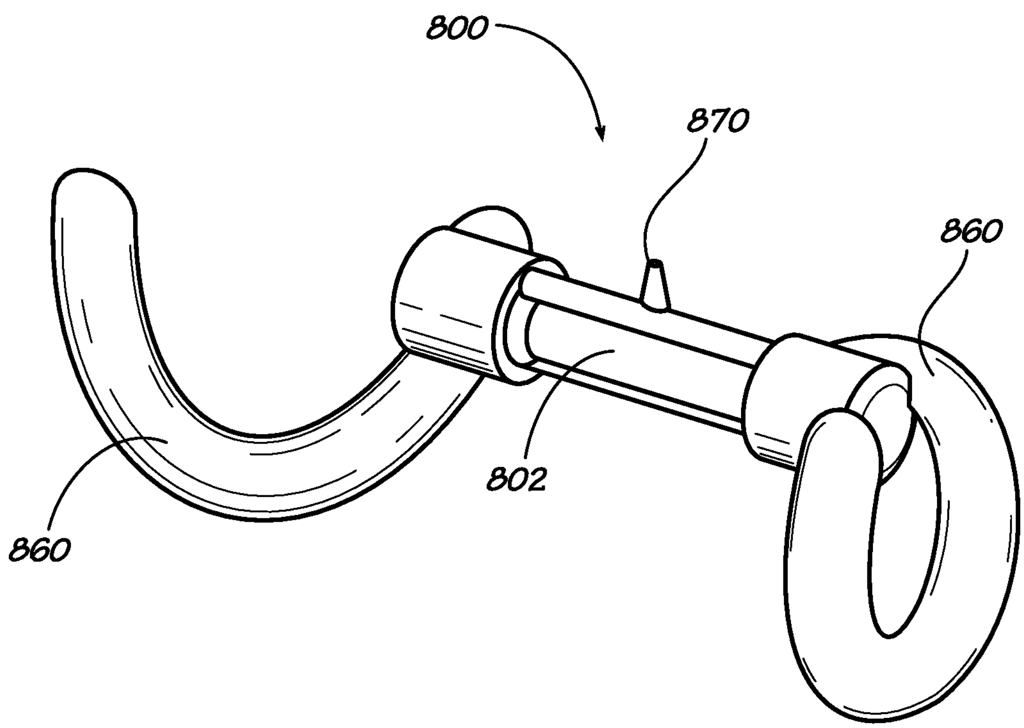


FIG. 8B

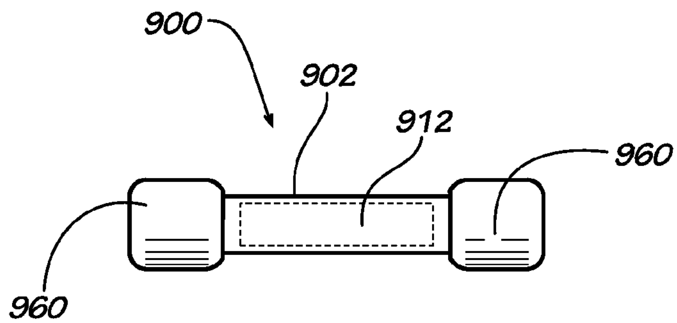


FIG. 9A

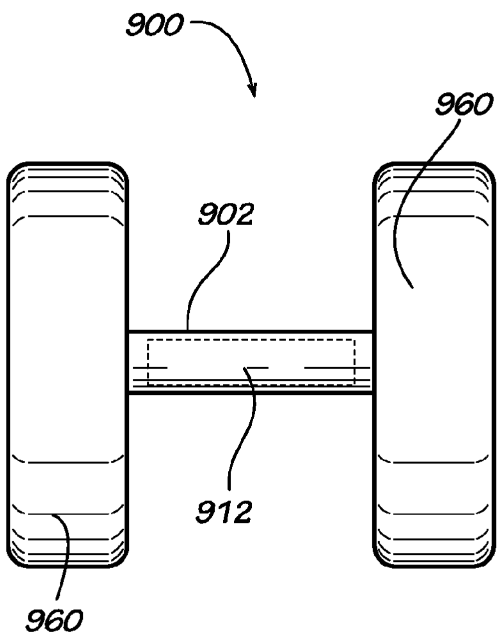


FIG. 9B

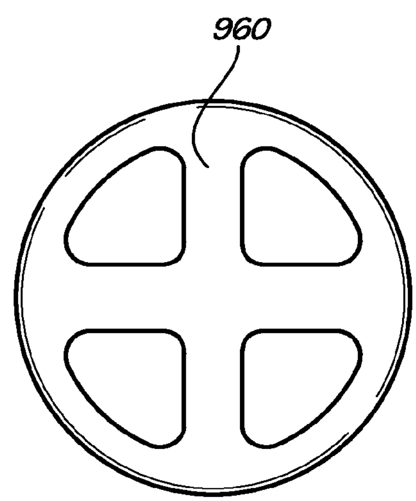
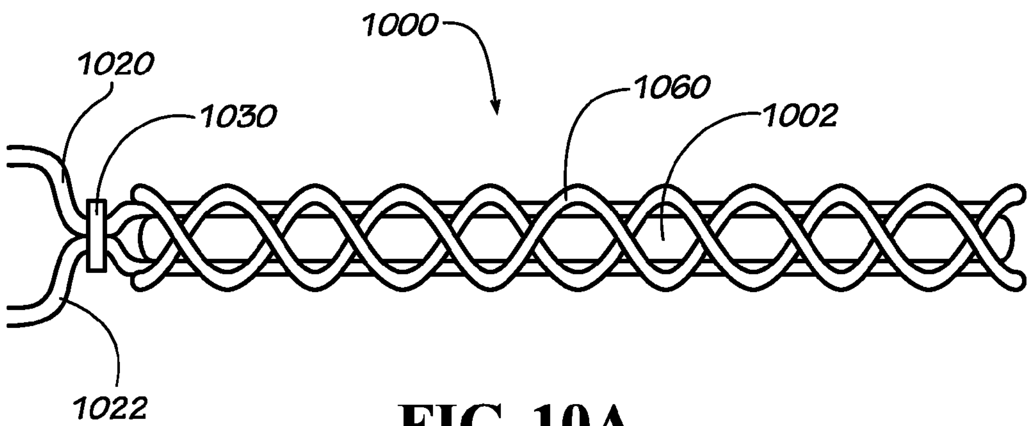


FIG. 9C



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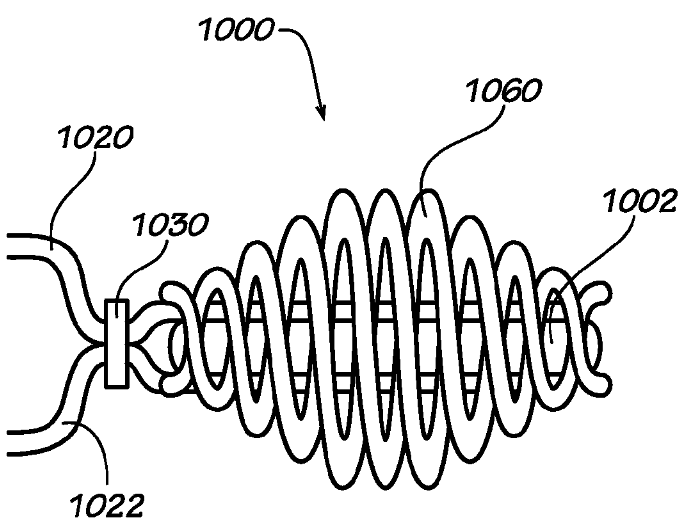

FIG. 10B

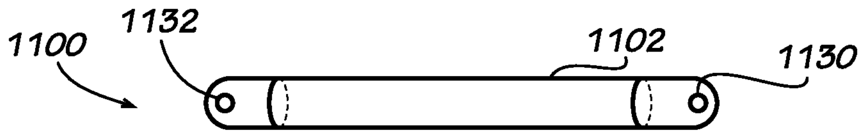

FIG. 11A

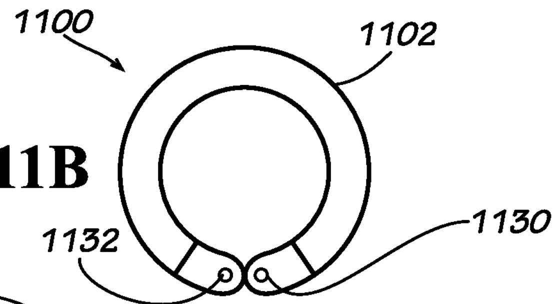

FIG. 11B

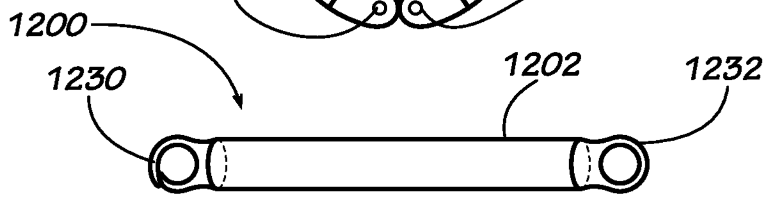

FIG. 12A

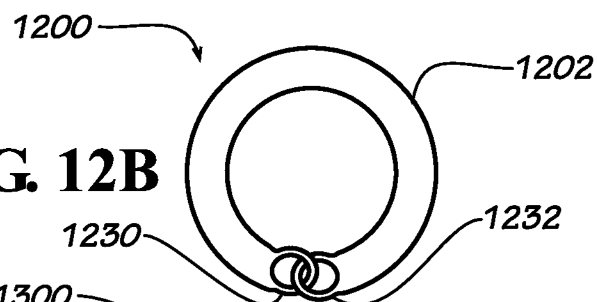

FIG. 12B

FIG. 13A

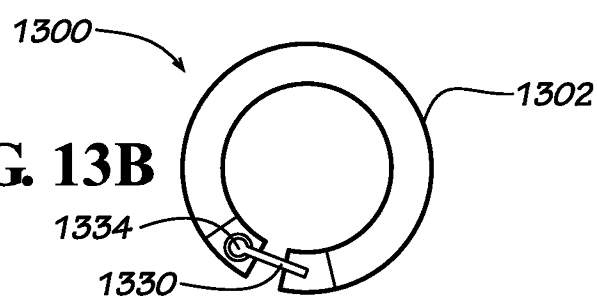

FIG. 13B

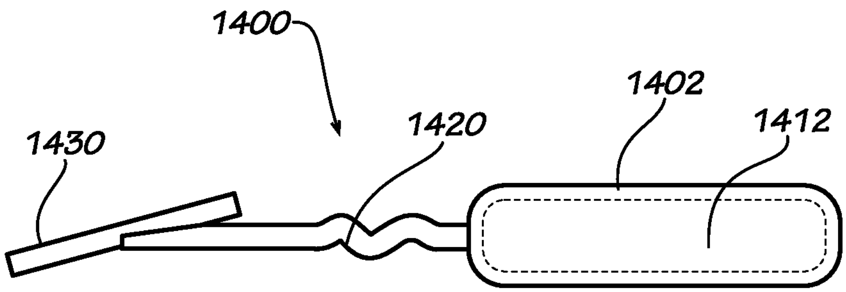

FIG. 14A

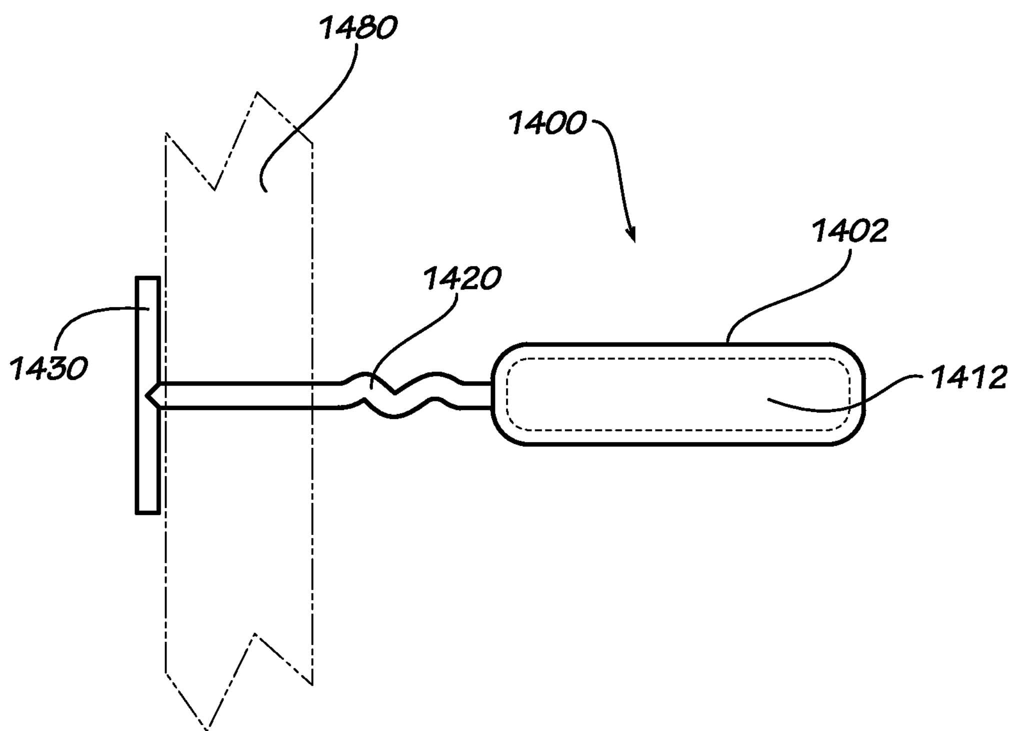

FIG. 14B

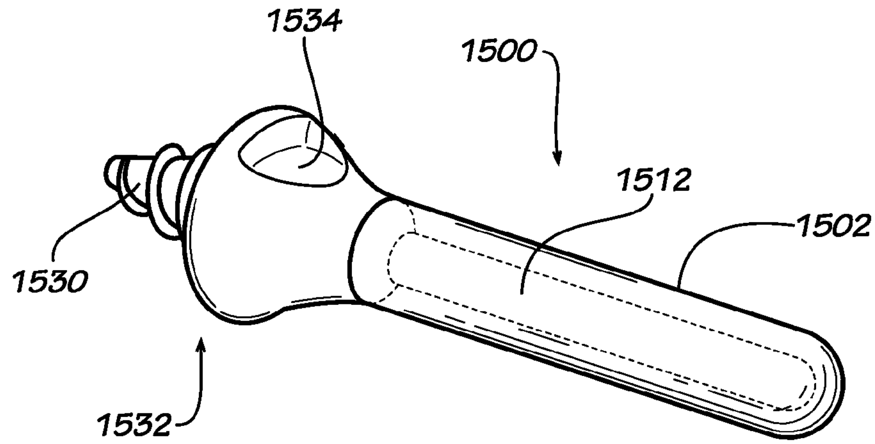

FIG. 15A

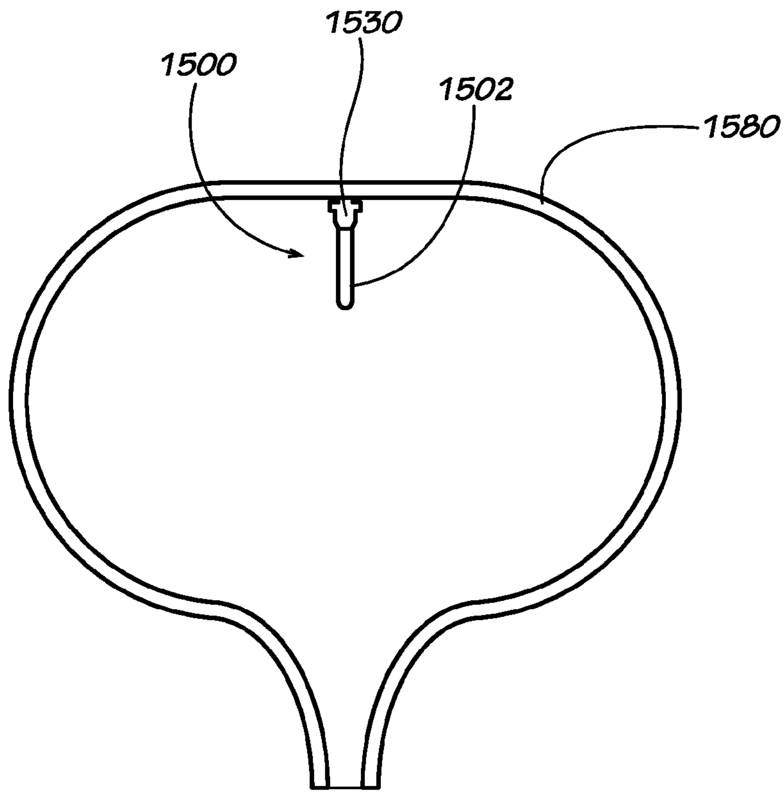

FIG. 15B

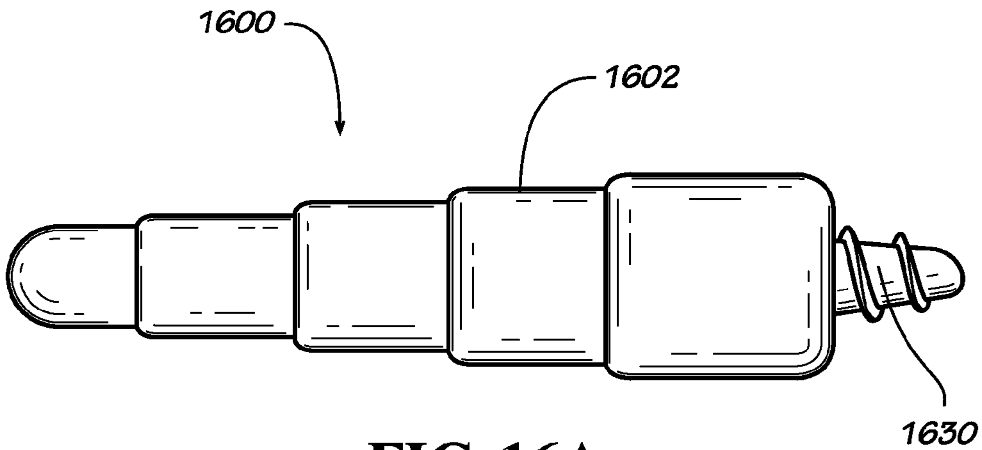

FIG. 16A

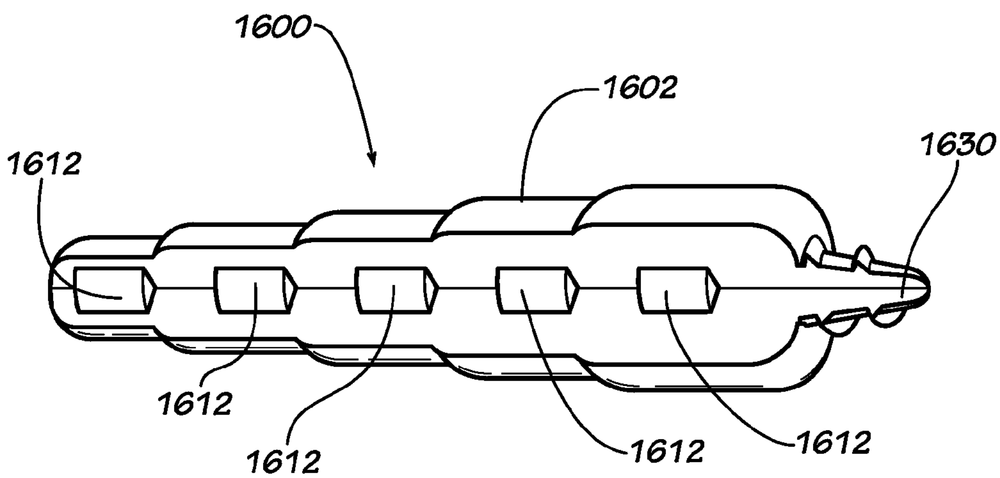

FIG. 16B

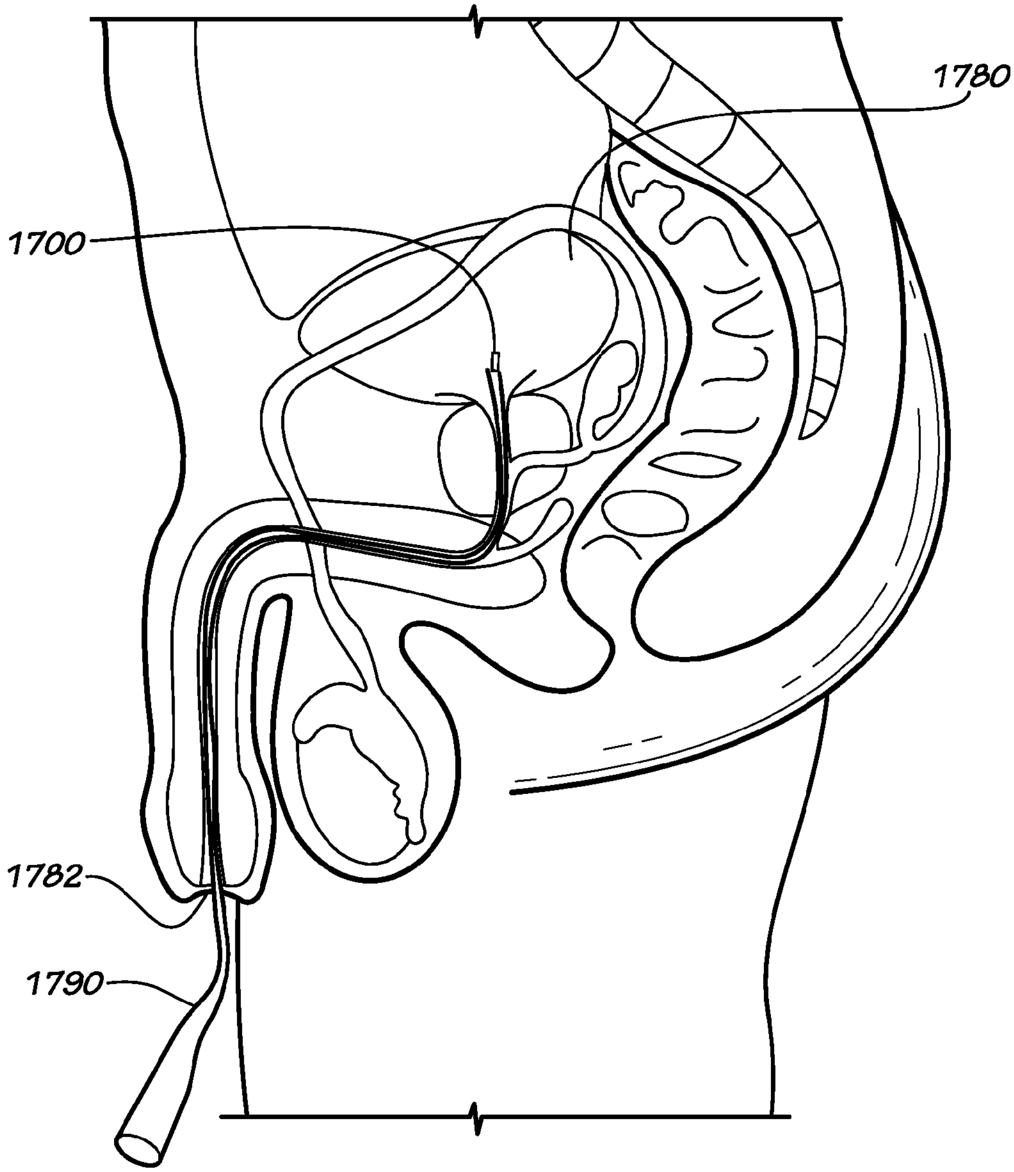

FIG. 17

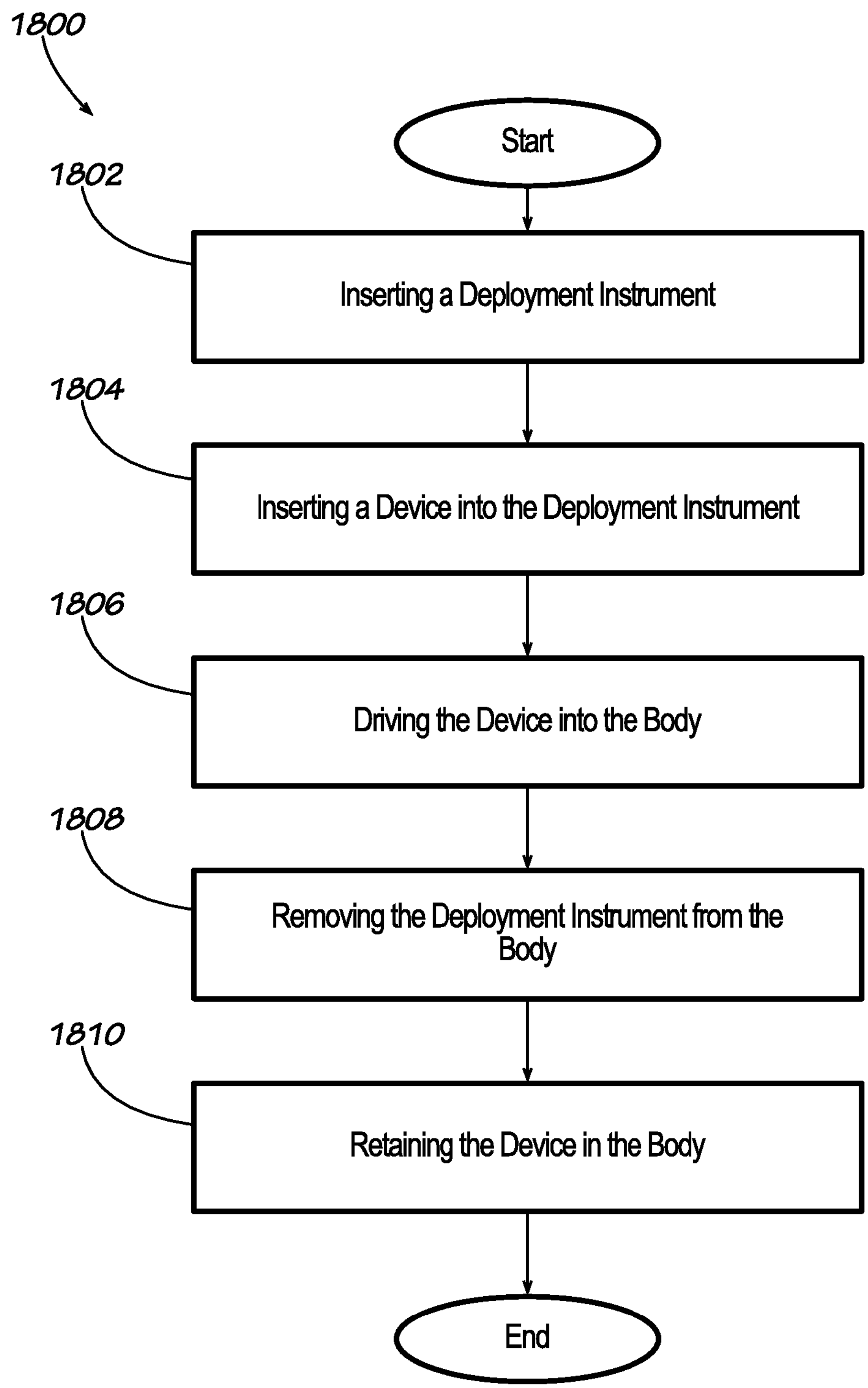
1800
1802
1804
1806
1808
1810
Start
Inserting a Deployment Instrument
Inserting a Device into the Deployment Instrument
Driving the Device into the Body
Removing the Deployment Instrument from the Body
Retaining the Device in the Body
End

FIG. 18

IMPLANTABLE DRUG DELIVERY DEVICES FOR GENITOURINARY SITES

BACKGROUND

The present disclosure generally relates to implantable medical devices, and more particularly relates to implantable devices for controlled drug delivery to the bladder and other genitourinary sites.

Systems for delivering drug locally to the bladder are known. For example, instillation permits delivering a solution of drug locally to the bladder, but drawbacks are present, such as the inability to achieve continuous drug delivery over an extended period. Continuous drug delivery can be achieved from implantable devices, but many implantable devices are not suited for the bladder. For example, some implantable devices are excreted from the bladder under the forces of urination, frustrating drug delivery. Also, many implantable devices cannot fit through the urethra, preventing minimally invasive deployment through this natural pathway. Other devices may fit through the urethra in an unfilled state but must be loaded with the drug after implantation. Furthermore, many known implantable devices cannot achieve sustained and controlled delivery of a therapeutically effective amount of drug over an extended period. For example, some known devices that are small enough to be deployed through the urethra are too small to hold a sufficiently large drug payload.

A need therefore exists for implantable devices that can be deployed through a natural orifice and/or lumen of the body into a body cavity, such as through the urethra into the bladder, and can be retained in the body under expected conditions, such as within the bladder during urination. Preferably the devices provide controlled release of one or more drugs for an extended period following implantation.

BRIEF SUMMARY

Implantable drug delivery devices are provided that have a deployment shape to facilitate implantation in the body and a retention shape or retention feature to facilitate retention in the body. The device may have one or more elongated drug reservoirs containing a drug, and the drug reservoir may be formed from a deformable material. In one embodiment, a first filament is attached to the first end of the drug reservoir and second filament is attached to the second end of the drug reservoir, wherein a fastener is positioned about the first and second filaments to permit shortening, and prevent lengthening of the filaments with reference to the ends of the drug reservoir, as a means for transforming the device from the implantation shape to the retention shape. This and other disclosed embodiments provided a device deployable through a natural orifice and/or lumen of the body into a body cavity, such as through the urethra into the bladder, and that can be retained in the body under expected conditions, such as within the bladder during urination, during a period of controlled release of one or more drugs.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** illustrates an embodiment of an implantable drug delivery device, FIG. **1**A illustrating the device in a deployment shape and FIG. **1**B illustrating the device in a retention shape.

FIG. **2** illustrates another embodiment of an implantable drug delivery device, FIG. **2**A illustrating the device in a deployment shape and FIG. **2**B illustrating the device in a retention shape.

FIG. **3** illustrates another embodiment of an implantable drug delivery device, FIG. **3**A illustrating the device in a deployment shape and FIG. **3**B illustrating the device in a retention shape.

FIG. **4** illustrates another embodiment of an implantable drug delivery device, FIG. **4**A illustrating the device in a deployment shape and FIG. **4**B illustrating the device in a retention shape.

FIG. **5** illustrates another embodiment of an implantable drug delivery device, wherein FIG. **5**A illustrates the device in a deployment shape. FIG. **5**B illustrates the device in a retention shape, and FIG. **5**C illustrates the device in an excretion shape.

FIG. **6** illustrates another embodiment of an implantable drug delivery device, FIG. **6**A illustrating the device in a deployment shape and FIG. **6**B illustrating the device in a retention shape.

FIG. **7** illustrates another embodiment of an implantable drug delivery device, FIG. **7**A illustrating the device in a deployment shape and FIG. **7**B illustrating the device in a retention shape.

FIG. **8** illustrates another embodiment of an implantable drug deli very device, FIG. **8**A illustrating the device in a deployment shape and FIG. **8**B illustrating the device in a retention shape.

FIG. **9** illustrates another embodiment of an implantable drug delivery device, wherein FIG. **9**A is a cross-sectional view of the device in a deployment shape. FIG. **9**B is a cross-sectional view of the device in an implanted shape, and FIG. **9**C is a side view of the device in the implanted shape.

FIG. **10** illustrates another embodiment of an implantable drug delivery device, FIG. **10**A illustrating the device in a deployment shape and FIG. **10**B illustrating the device in a retention shape.

FIG. **11** illustrates another embodiment of an implantable drug delivery device, FIG. **11**A illustrating the device in a deployment shape and FIG. **11**B illustrating the device in a retention shape.

FIG. **12** illustrates another embodiment of an implantable drug delivery device. FIG. **12**A illustrating the device in a deployment shape and FIG. **12**B illustrating the device in a retention shape.

FIG. **13** illustrates another embodiment of an implantable drug delivery device, wherein FIG. **13**A illustrates the device in a deployment shape and FIG. **13**B illustrates the device in an implanted shape.

FIG. **14** illustrates another embodiment of an implantable drug delivery device, wherein FIG. **14**A illustrates the device unanchored to the bladder wall and FIG. **14**B illustrates the device anchored to a portion of the bladder wall.

FIG. **15** illustrates another embodiment of an implantable drug delivery device, wherein FIG. **15**A illustrates the device unanchored to the bladder wall and FIG. **15**B illustrates the device anchored to a portion of the bladder wall.

FIG. **16** illustrates another embodiment of an implantable drug delivery device, wherein FIG. **16**A illustrates a plan view of the device and FIG. **16**B illustrates a cross-sectional view of the device.

FIG. **17** is a sagittal view of a male genitourinary system illustrating a drug delivery device being deployed into the bladder.

FIG. **18** is a block diagram illustrating an embodiment of a method for implanting an implantable device into the bladder.

DETAILED DESCRIPTION

Described herein are implantable devices that can be deployed through a natural orifice or lumen of the body into a body cavity and can be retained in the body cavity once implanted. In particular embodiments, the devices can deliver drug locally to the implantation site or regionally once implanted. For the purposes of the present disclosure, the term "implantation site" generally refers to a site within the body of a human patient or other animal. The implantation site can be any genitourinary site, such as the bladder, urethra, ureters, kidneys, prostate, seminal vesicles, ejaculatory duct, vas deferens, vagina, uterus, fallopian tubes, ovaries or any other location within a urological or reproductive system of the body, among other locations. In particular embodiments, the implantation site is the bladder.

Devices fix the bladder can be deployed through the urethra into the bladder in a minimally invasive deployment procedure. For example, the devices may be deployed through a deployment instrument, such as a catheter or cystoscope, that extends through the urethra to the bladder. Once implanted, the devices overcome the forces of urination to remain in the bladder, permitting drug delivery. Sustained and continuous delivery of an effective quantity of drug over an extended period may be enabled. The devices build upon those described in the following U.S. patent applications, which are incorporated by reference herein. U.S. application Ser. No. 11/461,956, filed Aug. 11, 2006; U.S. application Ser. No. 12/333,182, filed Dec. 11, 2008; U.S. application Ser. No. 12/538,580, filed Aug. 10, 2009; U.S. application Ser. No. 12/825,215, filed Jun. 28, 2010; U.S. application Ser. No. 12/825,238, filed Jun. 28, 2010; and U.S. Provisional Application No. 61/241,277, filed Sep. 10, 2009.

Embodiments of devices disclosed herein generally have at least one drug component. The drug component may include a drug and a drug reservoir. The drug may be in solid, semisolid, or liquid form, and the drug reservoir may be a tube or other hollow structure that houses the drug. The drug reservoir may at least partially shield the drug twin direct exposure to the implantation environment and may at least partially control release of the drug into the implantation environment.

The drug component also may be a solid drug form designed for extended release in response to direct exposure to the implantation environment. That is, the drug may be in a solid form that can be operably associated with a retention structure to provide controlled release of the therapeutic or prophylactic agent, without having a separate housing structure. For example, a therapeutic agent may be combined with (e.g., dispersed within) a matrix material in solid form and/or may have a controlled release coating thereon. The drug may be in the form of, for instance, a solid bead or disk that can be affixed to a retention structure.

The devices generally have a deployment shape suited for deployment, through a deployment instrument placed in the urethra or another natural lumen of the body. The deployment shape may be relatively elongated or linear. For example, the device may have a reduced width with reference to its length when in the deployment shape. Although the deployment shape facilitates deployment into the body, the deployment shape may increase the likelihood of excretion of the device from the body once implanted, such as during urination. Therefore, the devices are further configured for retention in the body.

Some device embodiments are retained in the body by assuming a retention shape. The device in the retention shape occupies a larger area or volume than the device in the deployment shape, reducing, the likelihood of excretion while permitting the device to free-float in the bladder. Other device embodiments are retained in the body by anchoring to a portion of the body, such as to the bladder wall. Anchoring prevents the device from free floating in the bladder, retaining the device in the bladder with reduced likelihood of excretion.

In certain embodiments, the device is associated with at least one retention structure. The retention structure may retain the device in the retention shape, or the retention structure may anchor the device to the body. Combinations of both retention modes are possible. Example retention structures include a string, wire, thread, cord, or other filament; a web, film, sheet, or other membrane; a balloon, basket, sponge, or other projection; two magnets, a hook and eye, a screw and threaded opening, or other fastener or lock; or a tether, screw, or other anchor, among others or combinations thereof.

In those embodiments in which the device achieves a retention shape, the retention structure may cause the drug component to achieve the retention shape or the retention structure itself may achieve the retention shape, either with or without changing the shape of the drug component. The retention structure may cause the device to automatically assume the retention shape once implanted, or the retention structure may be manipulated or manually adjusted after implantation to cause the device to assume the retention shape, such as with a medical instrument. The shape of the retention structure, the position of the retention structure with reference to the drug component, or both, may be altered to cause the device to assume the retention shape, and the retention structure may remain in the altered shape or position either naturally or under the influence of a fastener or lock.

For example, the retention structure may have a memorized shape that is spontaneously assumed upon implantation, such as in response to the temperature within or upon contact with urine in the bladder or in response to the removal of the confining force of the deployment instrument from the device upon escaping from the deployment instrument. Examples include a filament that can be deformed into an elongated shape for deployment and returns to a curved or coiled shape upon implantation, a membrane that can be rolled or folded into an elongated shape for deployment and returns to an expanded shape upon implantation, or a sponge that can be compressed into reduced space for deployment and expands upon exiting the deployment instrument into the bladder or upon contacting fluid therein.

The retention structure also may be manipulated or manually adjusted once the device is implanted to cause the device to assume the retention shape. Examples include a cord associated with the drug component that can be pulled to cause the drug component to change shape, a cord associated with multiple drug components that can be pulled to alter the position of the drug components with reference to each other, a filament or other structure that can be deformed into an expanded shape and maintains the shape once imparted, a balloon that can be filled, or a braided sleeve that can be expanded.

Some device embodiments are associated with an anchor structure that can anchor the device in the body, such as a movable tab, a threaded fastener, or a tether, among others. In embodiments in which the device is implanted in the bladder, the anchor structure may attach the device to the bladder wall so that the device is retained therein.

Specific embodiments will now be described by way of example. It should be understood that aspects of one of these embodiments can be combined with aspects of another of these embodiments to produce yet a further embodiment that is included within the scope of the present disclosure.

FIG. **1** illustrates an implantable drug delivery device **100**, wherein the drug component includes a drug reservoir **102** loaded with drug **112** and the retention structure includes two filaments **120**, **122** associated with a fastener **130**. As shown, the drug reservoir **102** is an elongated tube that can be deformed between a relatively linear deployment shape, such as the shape shown in FIG. **1**A, and a relatively circular retention shape, such as the shape shown in FIG. **1**B. The drug **112** may be loaded in the tube in a flexible form, so that the drug reservoir **102** can be moved between the two shapes. For example, the drug **112** may be a number of solid drug tablets, a liquid, or a gel. The filaments **120**, **122** may be attached to opposite ends of the drug reservoir **102** and joined by the fastener **130**. The fastener **130** can be adjusted to adjust the position of one filament **120** with reference to the other **122**, thereby adjusting the position of one end of the drug reservoir **102** with reference to the other end. The device **100** can assume the retention shape by adjusting the filaments **120**, **122** to draw the ends of the drug reservoir **102** closer together, and thereafter the device **1100** can be retained in the retention shape by preventing adjustment of the filaments **120**, **122** with the fastener **130**. In such an embodiment, the device **100** is manually adjusted into the retention shape hr manually adjusting the filaments **120**, **122** after the device **100** is implanted.

In the illustrated embodiment, the fastener **130** is a cinch nut that permits shortening the portion of the filaments **120**, **122** between the drug reservoir ends and the cinch nut but prevents lengthening of these portions of the filaments **120**, **122**. Thus, the ends of the drug reservoir **102** can be drawn closer together by pulling one or both of the filaments **120**, **122** through the cinch nut, causing the device **100** to assume the retention shape. Once the filaments **120**, **122** have been so adjusted, the cinch nut prevents lengthening of the filaments **120**, **122**, retaining the device in the retention shape. Thus, manually adjusting the device **100** into the retention shape once implanted merely requires pulling one or both of the filaments **120**, **122**, although other fasteners **130** that require separate manipulation can be employed. Other fasteners may also be used. Examples are shown below in FIGS. **11-13**.

To remove the device **100**, one or both of the filaments **120**, **122** may be snipped causing the drug reservoir **102** to return to the deployment shape. Thereafter, the device **100** may be pulled through the urethra. Alternatively, all or a portion of the device **100** can be formed of a bioresorbable (e.g., biodegradable or bioerodible) material. In one case, the degradation of the device is substantial enough that it negates the need for a removal procedure, as the degradation products can be excreted. In another case, the fastener **130**, filaments **120**, **122**, or a portion of the drug reservoir **102** is configured to degrade after a period (e.g., post drug release) to cause a break therein to release the tension holding the device **100** in the retention shape and permitting it to return to the deployment shape for retrieval through the urethra.

FIG. **2** illustrates an implantable drug delivery device **200**, wherein the drug component includes a number of drug reservoirs **202**, **204**, **206**, **208** loaded with drug, and the retention structure includes a filament **220** associated with a fastener **230**. As shown, the drug reservoirs **202**, **204**, **206**, **208** are elongated tubes that are joined at their ends with joints **240**, **242**, **244**, **246**. The drug components may not be flexible, meaning one or both of the drug reservoir **202**, **204**, **206**, **208** and the drug can be rigid. The joints **240**, **242**, **244**, **246**, however, are flexible, which permits adjusting the relative positions of the drug components with reference to each other. Thus, the device **200** can be adjusted between a relatively linear deployment shape, such as the shape shown in FIG. **2**A, and a relatively expanded retention shape, such as the square shape shown in FIG. **2**B.

To maintain the device **200** in the retention shape once so adjusted, the filament **230** extends from one of the joints **240** through an opening **250** in an opposite joint **246**. The filament has a locking bead positioned on it, which serves as the fastener **230**. The locking bead is positioned at an appropriate distance on the filament **220** such the locking bead is located within a boundary of the device **200** when the device is in the deployment shape and outside of the device boundary when the device **200** is in the retention shape. Although the locking bead is sized slightly larger than the opening **250**, the structure defining the opening **250** has sufficient flexibility such that the locking bead can pass through the opening **250** when the filament **230** is forcefully pulled. Thereafter, the opening **250** returns to a position that prevents passage of the locking bead, maintaining the relative positions of the drug reservoirs **202**, **204**, **206**, **208** to retain the device **200** in the retention shape. Thus, moving the device **200** from the deployment shape to the retention shape merely requires pulling the filament **220** until the locking bead passes through the opening **250**. It should be noted that four elongated, tubular drug reservoirs **202**, **204**, **206**, **208** are shown by way of example, although a different number or shape of drug reservoirs could be used. Further, the drug reservoirs **202**, **204**, **206**, **208** may be locked in position using a fastener **230** other than a filament associated with a locking bead.

FIG. **3** illustrates an implantable drug delivery device **300**, wherein the drug component includes a number of drug beads **302**, and the retention structure includes a filament **320**. The drug beads **302** are positioned along the filament **320**. The beads **302** provide controlled release of the drug in vivo. In one embodiment, the drug bead is in the form of a bioresorbable matrix material in which a drug is dispersed. In another embodiment, the bead may be a compressed drug tablet having a bioresorbable coating thereon. Five spherical drug beads **302** are shown in FIG. **3**, although any number or shape may be used. The drug beads **302** also could be substituted with drug, reservoirs housing a drug, or a combination of drug bead and drug reservoirs could be used to provide complementary drug release profiles (e.g., one or more units for immediate release with one or more units for delayed release).

The filament **320** is formed, from a shape-memory material that is preprogrammed to assume a retention shape but can be deformed or adjusted into other shapes. Thus, the device **300** can be adjusted into a relatively linear deployment shape, such as the shape shown in FIG. **3**A, and upon exiting the deployment instrument into the bladder, the device **300** automatically assumes the relatively expanded and curved retention shape, such as the shape shown in FIG. **3**B. It should be noted that the illustrated retention shape is merely one example. In other embodiments, the filament may be preprogrammed to assume other non-linear, expanded shapes. The filament **320** also may be formed from a material that does not have shape memory but instead can maintain an imparted shape once manipulated. In such cases, the filament is manually adjusted into the retention shape once implanted in the bladder.

FIG. **4** illustrates another implantable drug delivery device **400**, wherein the retention structure includes a filament **420** and the drug component includes drug reservoirs **402**, **404** loaded with drug **412** positioned on ends of the filament **420**. Two spherical drug reservoirs **402**, **404** are shown, although any number or shape may be used. The filament **420** may be formed from an elastic wire that is preprogrammed to assume a retention shape but can be deformed or adjusted into other shapes. Thus, the device **400** may adjusted into a relatively linear deployment shape, such as the shape shown in FIG. **4**A, and upon exiting the deployment instrument into the bladder, the device **400** may automatically assume the relatively expanded and curved retention shape, such as the shape shown in FIG. **4**B. The illustrated retention shape is merely one example, as the filament ma be preprogrammed to assume other non-linear, expanded shapes. The filament **420** also may be formed from a shape-memory material other than elastic wire, or from a material that does not have shape memory but instead can maintain an imparted shape once manipulated. In such cases, the filament may be manually adjusted into the retention shape in the bladder.

FIG. **5** illustrates an implantable drug delivery device **500**, wherein the drug component includes a drug disk **502**, and the retention structure includes a filament **520**. The drug disk **502** is positioned on the filament **520** such that ends or other portions of the filament **520** are embedded in the disk **502**. The drug disk **502** may be constructed with a bioresorbable matrix material and/or a coating to provide controlled release of the drug, much like the drug beads described above with reference to FIG. **4**. The filament **520** may be formed from a shape-memory material that is preprogrammed to assume a retention shape. Thus, the filament **520** may be adjusted into a relatively linear deployment shape, such as the shape shown in FIG. **5**A, and upon exiting the deployment instrument into the bladder, the filament **520** may automatically assume a relatively expanded retention shape, such as the "figure eight." shape shown in FIG. **5**B. Upon absorption of the drug disk **502**, the ends or other embedded portions of the filament **520** are released, causing the filament **520** to return to an elongated configuration, shown in FIG. **5**C, for excretion from the bladder. Thus, the device **500** may not require a medical procedure to be removed. It should be noted that, in other embodiments, the drug disk can have other shapes and the retention shape may be other than a figure eight.

FIG. **6** illustrates an implantable drug deliver device **600**, wherein the retention structure is a flexible web **620** and the drug components are embedded in the web. The web **620** may be deformed into a folded deployment shape, shown in FIG. **6**A, and upon exiting the deployment instrument into the bladder, the web may automatically assume the relatively flat at expanded shape shown in FIG. **6**B. For example, the flexible web **620** may be elastic and ma naturally have a substantially flat shape (in the absence of compressive forces). A relief opening **650** may or may not be provided in a central portion of the web **620** to facilitate folding and reduce bunching of the web **620** when in the deployment shape. The relief opening **650** also may permit urine to flow through the web **620** once implanted in the bladder. In certain embodiments, additional relief openings are provided through other portions of the web so that greater fluid flow is permitted. As shown, the web **620** may be somewhat star-shaped and the drug components may be elongated drug reservoirs **602** that extend radially outward about the web **620**. However, other web shapes and other drug reservoir numbers, shapes and positions can be used.

For example, FIG. **7** illustrates another implantable drug delivery device **700**, wherein the retention structure is a web **720** that is relatively circular in shape. The web **720** has elongated relief openings **750** formed through its surface, aligned with each other. The relief openings **750** are interspaced with drug reservoirs **702** loaded with drug **712** embedded in the web **720**. The web **720** may be rolled into a deployment shape, shown in FIG. **7**A, and upon exiting the deployment instrument into the bladder, the web **720** may automatically assume the relatively, flat expanded shape shown in FIG. **7**B.

In various embodiments of the devices shown in FIG. **6** and FIG. **7**, the web may be formed of a biocompatible flexible polymeric sheet. The sheet may be bioresorbable. The solid drug components may be attached to the outside surface(s) of the web, or they may be integrated into a drug reservoir formed in the web. For example, the drug reservoir may be in the form of a space formed entirely or partially by the web. In one case, the drug component is sandwiched between two thin sheets that are stacked and adhered together about a periphery of each drug component. In another case, the drug components are secured in grooves or within elongated apertures in the web. The drug components may be in the form of solid drug rods, which may be constructed of a bioresorbable matrix material (mixed with a drug) and/or a coating to provide controlled release of the drug. Such drug rods may be formed by casting or compression molding, for example, of drug alone or in combination with one or more binders or other excipients.

FIG. **8** illustrates another implantable drug delivery device **800**, wherein the drug component is a drug reservoir **802** loaded with drug, and the retention structure includes a number of inflatable balloons **860** in communication with an inflation port **870**. The drug component may be elongated and may or may not be deformable, either due to the rigidity of the drug reservoir **802** or the drug. When the balloons **860** are not inflated, the device **800** takes on a relatively linear deployment shape, such as the shape shown in FIG. **8**A, and when the balloons **860** are inflated, the device **800** assumes a retention shape, such as the shape shown in FIG. **8**B. The balloons may be inflated by directing a fluid (e.g., air, saline) through the inflation port **870** after the device **800** is implanted. In the illustrated embodiment, two balloons **860** are positioned on opposite ends of the drug reservoir **802**, and the balloons **860** assume arched or hooked shapes upon inflation, although other numbers, positions, and inflated shapes can be used. The inflated balloons **860** may advantageously enhance the buoyancy of the device **800** within the bladder.

FIG. **9** illustrates another implantable drug delivery device **900**, wherein the drug component is a drug reservoir **902** loaded with drug **912**, and the retention structure includes a number of sponges **960**. The drug component may be elongated and may or may not be deformable, either due to the rigidity of the drug reservoir **902** or the drug **912**. The sponges **960** may be capable of assuming a reduced volume, either when compressed or in a dehydrated state. When the sponges **960** are compressed, or are in a dehydrated state, the device **900** takes on a relatively linear deployment shape, such as the shape shown in FIG. **9**A, and when the sponges **960** are expanded, or hydrated, the device **900** assumes a retention shape, such as the shape shown in FIG. **9**B. The sponges **960** may automatically expand upon exiting the deployment instrument or in response to contacting and absorbing fluid in the bladder. In the illustrated embodiment, two sponges **960** are positioned on opposite ends of the drug reservoir **902**, and the sponges **960** assume wheel shapes upon expansion, although other numbers, positions, and expanded shapes can be used. In some embodiments, the sponges may be formed of a bioresorbable material that after swelling will degrade over time.

FIG. **10** illustrates an implantable drug delivery device **1000**, wherein the drug component includes a drug reservoir **1002** loaded with drug and the retention structure includes a braided basket **1060** associated with two filaments **1020**, **1022** and a fastener **1030**. The drug reservoir **1002** is an elongated tube that can be compressed along its length, much like a bellows. The drug may be loaded in the drug reservoir **1002** in a flexible form, so that the drug reservoir **1002** can be compressed along its length. For example, the drug may be a number of solid drug tablets, a liquid, or a gel. The braided basket **1060** may be positioned about the exterior of the drug reservoir **1002**, attached to the drug reservoir **1002** via the filaments **1020**, **1022**, which extend along opposite sides of the drug reservoir **1002** between the drug reservoir **1002** and the braided basket **1060**. The filaments **1020**, **1022** are joined together at one end of the device **1000** with the fastener **1030**.

The device **1000** generally assumes an elongated deployment shape, shown in FIG. **10**A. Once implanted the filaments **1020**, **1022** can be pulled to reduce the length of the drug reservoir **1002**, causing the braided basket **1060** to expand outward about its exterior, such that the device **1000** assumes the retention shape shown in FIG. **10**B. Thereafter the device **1000** can be retained in the retention shape by preventing adjustment of the filaments **1020**, **1022** with the fastener **1030**. In such an embodiment, the device **1000** is manually adjusted into the retention shape by manually adjusting the filaments **1020**, **1022** after the device **1000** is implanted.

In the illustrated embodiment, the fastener **1030** is a cinch nut that permits shortening but prevents lengthening the filaments **1020**, **1022**. Thus, the braided basket **1060** and drug reservoir **1002** can be drawn into a reduced length by pulling the filaments **1020**, **1022** through the cinch nut, causing the device **1000** to assume the retention shape. Once the filaments **1020**, **1022** have been so adjusted, the cinch nut prevents lengthening of the filaments **1020**, **1022**, retaining the device **1000** in the retention shape. Thus, manually adjusting the device **1000** into the retention shape once implanted merely requires pulling the filaments **1020**, **1022**, although other fasteners that require separate manipulation can be employed.

To remove the device **1000**, the filaments **1020**, **1022** may be snipped, causing the drug reservoir **1002** to return to the deployment shape. Thereafter, the device **1000** may be pulled through the urethra. Alternatively, all or a portion of the device **1000** can be formed of a bioresorbable material, such as described above with reference to FIG. **1**, so that a retrieval procedure is unnecessary.

FIGS. **11**-**13** illustrate implantable drug delivery devices **1100**, **1200**, **1300**, wherein the drug component is a drug reservoir **1102**, **1202**, **1302** loaded with drug, and the retention structure is a two-part fastening or locking device having its two parts positioned on opposite ends of the drug reservoir. For example, the two-part fastening or locking device can be two magnets **1130**, **1132** associated with opposite ends of the drug reservoir **1102**, as shown in FIG. **11**, a hook **1230** and an eye loop **1232** associated with opposite ends of the drug reservoir **1202**, as shown in FIG. **12**, or a screw **1330** and threaded opening **1332** associated with opposite ends of the drug reservoir **1302**, as shown in FIG. **13**. The drug reservoir **1102**, **1202**, **1302** is an elongated tube that can be deformed between a relatively linear deployment shape, shown in FIGS. **11**A, **12**A, and **13**A, and a relatively circular retention shape shown in FIGS. **11**B, **12**B, and **13**B. Once the device **1100**, **1200**, **1300** is implanted, the two parts of the two-part fastening device can be associated with each other to maintain the device **1100**, **1200**, **1300** in the retention shape. For example, the magnets **1130**, **1132** can be joined together as shown in FIG. **11**B, the hook **1230** can be attached to the eye loop **1232**, as shown in FIG. **12**B, and the screw **1330** can be threaded into the threaded opening **1332**, as shown in FIG. **13**B. In particular, the screw **1330** is engaged about a central portion and is rotated to thread the screw **1330** into the threaded opening **1332**, as the bead **1334** of the screw may be housed in a cavity in the drug reservoir **1302** that is sized and shaped to permit free rotation of the head **1334** with reference to the drug reservoir **1302**.

FIG. **14** illustrates an implantable drug delivery device **1400**, wherein the drug component is a drug reservoir **1402** loaded with drug **1412**, and the retention structure is an anchor **1430** connected via tether **1420** to the drug reservoir **1402**. The anchor **1430** may be T-shaped and may fold downward for deployment through the deployment instrument into the bladder, as shown in FIG. **14**A. Once in the bladder, the anchor **1430** engages the bladder wall **1480** to anchor the device **1400** therein, as shown in FIG. **14**B. Anchors with other configuration may be used, or the anchor ma be omitted completely, in which case the tether may be attached to the bladder wall using a mucoadhesive material known in the art. In some embodiments, the anchor **1430** may be bioresorbable so that the anchor **1430** does not need to be removed, in which case the device **1400** can be removed by cutting the tether **1420** and extracting the drug reservoir **1402** from the bladder. Alternatively, the drug reservoir **1402** also may be bioresorbable, or the drug reservoir **1402** may be substituted with a solid drug form that is not housed in a drug reservoir. The tether **1420** may be either bioresorbable or excretable, so that the device **1400** is completely resorbable or does not otherwise require separate removal.

FIG. **15** illustrates an implantable drug delivery device **1500**, wherein the drug component is a drug reservoir **1502** loaded with drug **1512**, and the retention structure is a threaded anchor **1530** positioned on one end of the drug reservoir **1502**. The entire device **1500** may be elongated, as shown in FIG. **15**A, for deployment through a deployment instrument. Once in the bladder, the anchor **1530** may threadingly engage the bladder wall **1580** to anchor the device therein, as shown in FIG. **15**B. In some embodiments, the threaded anchor **1530** may be configured for easy grasping with an insertion instrument. For example, the threaded anchor **1530** may be attached to the drug reservoir **1502** at a head portion **1532**, which may include detents **1534** that facilitate engaging the device **1500** with forceps or another insertion tool. The threaded anchor **1530** also may be omitted, in which case the drug reservoir **1502** may be attached to the bladder wall using a mucoadhesive material.

FIG. **16** illustrates an implantable drug delivery device **1600**, wherein the drug component includes a drug reservoir **1602** housing a number of drug doses **1612**, and the retention structure is a threaded anchor **1630** positioned on one end of the drug reservoir **1602**. The entire device **1600** may be elongated, as shown in FIG. **16**A, for deployment through a deployment instrument. Once in the bladder, the threaded anchor **1630** may threadingly engage the bladder wall to anchor the device **1600** therein. The drug reservoir **1602** is formed from a bioresorbable material that can degrade in the implantation environment. The drug reservoir **1602** is shaped so that the material thickness increases along, the length of the device **1600**, either uniformly or in a stepped fashion as shown in FIG. **16**A. A number of drug doses **1612** are housed within the material, as shown in FIG. **16**B, and the drug doses **1612** are exposed as the material degrades. Because the drug reservoir **1602** degrades at a varying rate along the length of the device **1600** due to the variation in material thickness, the drug doses **1612** are released at varying rates.

FIG. **17** is a sagittal view of a male genitourinary system, illustrating an implantable drug delivery device **1700** being deployed through a deployment instrument **1790** into an implantation site. By way of example, the male anatomy is shown and the implantation site is shown as the bladder **1780**. The drug delivery device **1700** may be an embodiment of one of the implantable drug delivery devices described herein. The deployment instrument **1790** may be any device designed to navigate natural lumens of the body to reach the intended implantation site. For deployment in the bladder **1780**, the deployment instrument **1790** is sized and shaped for passing through a urethra **1782** of a patient to a bladder **1780** as shown. The deployment instrument **1790** may be a known device, such as a catheter or cystoscope, or a specially designed device, such as an one of the deployment instruments described in U.S. Provisional Application No. 61/241,229, filed on Sep. 10, 2009, or U.S. Provisional Application No. 61/311,103, filed on Mar. 5, 2010, each of which is incorporated herein by reference. The deployment instrument **1790** is used to deploy the implantable device **1700** into the body and is subsequently removed from the body, leaving the implantable device **1700** wholly implanted in the body, either free-floating therein or anchored thereto. Once so implanted, the device **1700** may release drug into the body for an extended period. A comparable procedure can be used to deploy any of the devices described herein into other pans of the body through other natural lumens.

FIG. **18** is a block diagram illustrating an embodiment of a method **1800** for implanting an implantable device into the bladder, such as an embodiment of one of the implantable drug delivery devices described herein. In block **1802**, a deployment instrument is inserted into the body. The deployment instrument may be inserted into the urethra and driven forward until a distal end of the deployment instrument is positioned in the bladder while a proximal end remains outside of the body.

In block **1804**, the device is inserted into the deployment instrument. In some cases, inserting the device into the deployment instrument can include deforming the device from a retention shape to a deployment shape. In some cases, the order of blocks **1802** and **1804** is reversed.

In block **1806**, the device is driven into the bladder. Driving the device from the deployment instrument removes the force of the deployment instrument wall from the device, which may cause the device to naturally return to a retention shape for retention in the bladder. Alternatively, the device may be manipulated into a retention shape or the device may be anchored in the bladder.

In block **1808**, the deployment instrument is removed from the body. Thereafter, in block **1810**, the device is retained within the body. The device either free floats in the bladder or is anchored therein to the bladder wall. The device may be retained for an extended period, such as a period of hours, days, weeks, or months. In embodiments in which the device is an implantable drug delivery device, the device remains implanted to release drug from the device into the bladder, such as to the urothelial tissues and other local or regional tissues. Subsequently, the device may be removed or resorbed.

The devices described herein can be used to deliver essentially any drug or combination of drugs for treatment or prophylaxis of a variety of conditions and diseases. In a certain application, the devices are useful for treatment of genitourinary tissue sites. In one embodiment, the implantable drug delivery device is used to provide pain relief to the patient. In other embodiments, the drug delivery device is used to treat inflammatory conditions such as interstitial cystitis, radiation cystitis, painful bladder syndrome prostatitis, urethritis, post-surgical pain, and kidney stones, in still other embodiments, the drug delivery device is used to treat urinary incontinence, frequency, or urgency, including urge incontinence and neurogenic incontinence, as well as trigonitis. In yet another embodiment, the drug delivery device is used to treat urinary tract cancer, such as bladder cancer and prostate cancer. In still another embodiment, the drug delivery device is used to treat infections involving the bladder, the prostate, and the urethra. In other embodiments, the drug delivery device is used to treat fibrosis of a genitourinary site, such as the bladder or uterus. Drugs suitable for use in the implantable drug delivery devices described herein are known in the art and/or are described in the patent applications that are cited above and incorporated herein by reference.

Publications cited herein and the materials for which they are cited are specifically incorporated herein by reference. Modifications and variations of the methods and devices described herein that are obvious to those skilled in the art from the foregoing detailed description are intended to conic within the scope of the appended claims.

We claim:

1. An implantable drug delivery device, comprising:
a drug reservoir, the drug reservoir having an elongated shape, the drug reservoir formed from a deformable material;
a drug loaded in the drug reservoir;
a first filament attached to a first end of the drug reservoir;
a second filament attached to a second end of the drug reservoir; and
a fastener positioned about the first and second filaments, the fastener permitting shortening and preventing lengthening of the filaments with reference to the ends of the drug reservoir.

2. The implantable drug delivery device of claim **1**, wherein the fastener comprises a cinch nut.

3. The implantable drug delivery device of claim **1**, wherein the fastener is adjustable to enable the device to be deformed from a relatively linear deployment shape to a relatively circular retention shape.

4. An implantable drug delivery device comprising:
a plurality of drug reservoirs;
a drug loaded in the drug reservoirs;
a plurality of flexible joints joining the drug reservoirs together at their ends, at least one of the flexible joints having an opening;
a filament extending from one of the flexible joints through the opening; and
a fastener positioned on the filament, the fastener being movable through the opening upon engagement of the filament to lock the drug reservoirs in a retention shape.

5. The implantable drug delivery device of claim **4**, wherein the fastener comprises a locking bead.

6. An implantable drug delivery device comprising:
a bellows-shaped drug reservoir;
a drug loaded in the drug reservoir;
a braided basket positioned about the drug reservoir;
two filaments positioned between the drug reservoir and the braided basket, attached to both; and
a fastener associated with the filaments, wherein the device can be moved into a retention shape of increased width and reduced length by pulling the filaments through the fastener, causing the basket to expand outward.

7. A method of administering a drug to a patient in need thereof, comprising:
deploying the implantable drug delivery device of claim **1** into the patient; and
releasing from the deployed device one or more drugs into the patient.

8. The method of claim **7**, wherein the step of deploying an implantable drug delivery device comprises deploying the device through a deployment instrument into the patient's bladder.

9. A method of administering a drug to a patient in need thereof, comprising:
deploying the implantable drug delivery device of claim **4** into the patient; and

releasing from the deployed device one or more drugs into the patient.

10. The method of claim **9**, wherein the step of deploying an implantable drug delivery device comprises deploying the device through a deployment instrument into the patient's bladder.

11. A method of administering a drug to a patient in need thereof, comprising:

deploying the implantable drug delivery device of claim **6** into the patient; and

releasing from the deployed device one or more drugs into the patient.

12. The method of claim **11**, wherein the step of deploying an implantable drug delivery device comprises deploying the device through a deployment instrument into the patient's bladder.

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